

REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office Action dated April 27, 2010 are respectfully requested.

I. Amendments

Claim 1 is amended to recite the vesicle anchored to the lipid bilayer through complementary oligonucleotides includes a receptor having a binding site located on the exterior of the vesicle and is capable of specifically binding a test agent. Basis for this amendment can be found, for example, on page 11, lines 25-29 and in Fig. 10.

New claims 22-23 find basis on page 11, lines 30-32.

New claims 24-25 find basis on page 24, lines 21-22

No new matter is added by way of these amendments.

II. Rejections under 35 U.S.C. §103

Claims 1-4, 6, 7, 9, and 11-12 were rejected under 35 U.S.C. §103 as allegedly obvious over Boxer *et al.* (PCT Publication No. WO 98/23948) in view of both Boukobza *et al.* (*J Phys Chem*, 105:12165-12170, 2001) and Niemeyer *et al.* (DE 19902391).

Claims 1-4, 6, 7, and 9-12 were rejected under 35 U.S.C. §103 as allegedly obvious over Boxer *et al.* taken with both Boukobza *et al.* and Niemeyer *et al.*, in further view of each of Cornell *et al.* (U.S. Patent No. 5,874,316), Arnold *et al.* (U.S. Patent No. 5,310,648), or Bayerl *et al.* (U.S. Patent No. 6,051,372).

Claims 1-4, 6-9, 11, and 12 were rejected under 35 U.S.C. §103 as allegedly obvious over Boxer *et al.* taken with both Boukobza *et al.* and Niemeyer *et al.*, in further view of Shen *et al.* (U.S. Publication No. 2003/0148335).

These rejections are respectfully traversed.

A. The Present Claims

Independent claim 1 relates to an array of separated lipid bilayers. The array includes a plurality of discrete lipid bilayer expanses on a substrate, each expanse contains one or more lipids derivatized with an oligonucleotide having a surface region

specific sequence and at least one biomolecule anchored to at least one of the lipid bilayer expanses through a complementary oligonucleotide sequence capable of specifically hybridizing with the surface region specific oligonucleotide sequence in that expanse, such that the biomolecule is anchored to that expanse. One or more of the biomolecules is a vesicle capable of specifically binding a test agent. The vesicle includes at least one receptor associated with the vesicle. The receptor has a binding site located on the exterior of the vesicle and is capable of specifically binding a test agent.

A challenge to using lipid bilayer arrays on a solid substrate for large proteins such as receptors is that the protein may extend beyond the lipid bilayer and interact with or drag on the substrate. This interaction can cause denaturation and loss of function of the protein or limit the lateral mobility of the lipid bilayer on the substrate. By having the vesicle tethered to the bilayer expanse through complementary oligonucleotides as in the present claims, the vesicle and associated receptor are distanced from the substrate. Therefore, the presently claimed array retains the benefits of spatial organization and lateral mobility from the lipid bilayer on a substrate while retaining the function of the receptor.

B. The Cited References

BOXER ET AL. relate to a surface detector array formed of a substrate having a surface defining a plurality of distinct bilayer-compatible surface regions separated by one or more bilayer barrier regions. The bilayer-compatible surface regions may further include a selected biomolecule covalently or non-covalently attached to a lipid molecule (see page 4 line 32 through page 5, line 2). Examples of biomolecules include polynucleotides and nucleic acids (see page 5, lines 4-5 and page 16, line 4). The bilayer may be derivatized with groups or compounds to create a surface having the desired surface exemplified by a ligand bound to the surface of the lipid by attachment to surface lipid components (see page 11, line 32 through page 12, line 2). Specific high-affinity molecular interactions may be employed to link biomolecules to a supported layer (see page 18, lines 7-8).

BOUKOBZA ET AL. describe an immobilization technique using biotin-avidin interaction. Large unilamellar lipid vesicles (LUV) are attached to a glass-supported lipid bilayer through the biotin-avidin binding interaction. The LUV includes a single biomolecule encapsulated inside the LUV for characterization of the biomolecule.

NIEMEYER ET AL. states reversible, parallel, site-specific immobilization of macromolecules on a solid phase comprising using nucleic acids as immobilization-mediating reagents. The components to be immobilized on the solid support are coupled with nucleic acids and the solid phase are functionalized with nucleic acids complementary thereto.

CORNELL ET AL. relate to receptor binding of an analyte.

ARNOLD ET AL. describe an imprinted matrix which exhibits selective binding interactions through metal chelates.

BAYERLE ET AL. describe two-dimensional patterning of a three-dimensional surface by a template molecule.

C. Analysis

To support an obviousness rejection, MPEP §2143.03 requires "all words of a claim to be considered" and MPEP § 2141.02 requires consideration of the "[claimed] invention and prior art as a whole." Further, the Board of Patent Appeal and Interferences recently confirmed that a proper, post-KSR obviousness determination still requires the Office make "a searching comparison of the claimed invention – including all its limitations – with the teaching of the prior art." *Ex parte Wada and Murphy*, Appeal 2007-3733 (2008), citing *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995) and *CFMT v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003). "It is well settled that the 'Patent and Trademark Office (PTO) must consider all claim limitations when determining patentability of an invention over the prior art.'" *Ex parte Wada and Murphy*, Appeal 2007-3733 (2008), citing *In re Lowry*, 32 F.3d 1579, 1582 (Fed. Cir. 1994).

1. Rejection over Boxer et al. taken with both Boukobza et al. and Niemeyer et al.

The combined teachings of Boxer et al., Boukobza et al. and Niemeyer et al. fail to satisfy the legal standard for a prima facie case of obviousness because the

combination fails to show or suggest the claimed array as a whole. Specifically, the combination fails to show or suggest an array of separated lipid bilayer expanses including at least one vesicle including a receptor associated therewith, the vesicle anchored to a lipid bilayer expanse through complementary oligonucleotides.

Boxer *et al.* describe a lipid bilayer array with a biomolecule attached to a lipid of the lipid bilayer but make no mention of the biomolecule being a vesicle. Boukobza *et al.* teach using biotin-avidin affinity for tethering a lipid vesicle having an entrapped biomolecule to a surface supported lipid bilayer. As seen in Figure 1 on page 12166, Boukobza *et al.* describes a liposome that includes a protein encapsulated within the liposome. However, the liposome of Boukobza *et al.* does not teach or suggest a vesicle including at least one receptor associated with the vesicle and having a binding site located on the exterior of the vesicle and being capable of specifically binding a test agent. Instead, the liposome is used to confine a single biomolecule within the liposome for fluorescence studies of the biomolecule. Nor would one modify Boukobza *et al.* to include a receptor having a binding site located on the exterior of the vesicle as Boukobza *et al.* is concerned with immobilization of the biomolecule so that it can be studied by single-molecule fluorescence. Such a procedure uses long measurement times and thus the molecule must be immobilized. Entrapment within the liposome allows the molecule to be immobilized within the liposome but retain freedom of motion for fluorescence polarization (see Abstract). Niemeyer *et al.* teaches immobilization of a biomolecule, which may be a vesicle, to a solid support through complementary oligonucleotide sequences. However, Niemeyer *et al.* makes no mention of including a receptor associated with the vesicle having a binding site located on the exterior of the vesicle and being capable of specifically binding a test agent. Therefore, this reference combined with Boxer *et al.* and/or with Boukobza *et al.* does not show or suggest all the features of claim 1.

At most, the combination of references taken as a whole can be said to teach a bilayer array as in Boxer *et al.* with a vesicle immobilized to the bilayer array through complementary nucleic acids as in Niemeyer *et al.* and Boukobza *et al.*, in part. Nowhere does the combination show or suggest anchoring a vesicle having at least one receptor having a binding site located on the exterior of the vesicle and being capable of

specifically binding a test agent above the lipid bilayer using complementary oligonucleotides so that the vesicle and/or receptor does not interact with the substrate.

2. Rejection over Boxer *et al.* taken with Boukobza *et al.* and Niemeyer *et al.*, in further view of Cornell *et al.*, Arnold *et al.*, or Bayerl *et al.*

The Examiner cites Cornell *et al.*, Arnold *et al.*, and Bayerl *et al.* for the sole purpose of providing features of dependent claim 10. Thus, for the prima facie case of obviousness to stand, the combined teachings of Boxer *et al.*, Boukobza *et al.* and Niemeyer *et al.* must provide all of the features of independent claim 1. For the reasons given above, it is abundantly clear that the combined teachings of Boxer *et al.*, Boukobza *et al.* and Niemeyer *et al.* do not provide all of the features of claim 1. Therefore, a prima facie case of obviousness of claim 10 has not been established.

3. Rejection over Boxer *et al.* taken with Boukobza *et al.* and Niemeyer *et al.*, in further view of Shen *et al.*

The Examiner cites Shen *et al.* for the sole purpose of providing features of dependent claim 8. Thus, for the prima facie case of obviousness to stand, the combined teachings of Boxer *et al.*, Boukobza *et al.* and Niemeyer *et al.* must provide all of the features of independent claim 1. For the reasons given above, it is abundantly clear that the combined teachings of Boxer *et al.*, Boukobza *et al.* and Niemeyer *et al.* do not provide all of the features of claim 1. Therefore, a prima facie case of obviousness of claim 8 has not been established.

As the references, alone or in combination, fail to teach or suggest all the claim limitations, the Examiner has failed to establish a prima facie case of obviousness. Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103.

III. Conclusion

In view of the foregoing, the claims pending in the application are in condition for allowance. A Notice of Allowance is, therefore, respectfully requested. If the Examiner

has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (650) 590-1939.

Respectfully submitted,
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Date: October 27, 2010

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